

claims

1. A method for identifying an antagonist or inhibitor of the expression of a gene encoding a polypeptide essential for bacterial growth or survival wherein said gene is selected from the group consisting of ygbB, yfhC, yacE, ychB, yejD, yrfI, yggJ, yjeE, yiaO, yrdC, yhbC, ygbP, ybeY, gcpE, kdtB, pfs, ycaJ, b1808, yeaA, yagF, b1983, yidD, yceG and/or yjbC, the sequence of said genes being shown in Fig. 1, or a fragment, derivative or ortholog thereof, said method comprising the steps of
 - (a) testing a candidate antagonist or inhibitor or a sample comprising a plurality of said candidate antagonists or inhibitors for the inhibition or reduction of transcription of said gene or a fragment or derivative thereof; or
 - (b) testing a candidate antagonist or inhibitor or a sample comprising a plurality of said candidate antagonists or inhibitors for the inhibition or reduction of translation of mRNA transcribed from said gene or a fragment or derivative thereof; and
 - (c) identifying an antagonist or inhibitor or a sample comprising a plurality of said candidate antagonists or inhibitors that tests positive in step (a) and/or (b).
2. A method for testing a candidate antagonist or inhibitor or sample of a polypeptide or a mRNA essential for bacterial growth or survival encoded by a gene selected from the group consisting of ygbB, yfhC, yacE, ychB, yejD, yrfI, yggJ, yjeE, yiaO, yrdC, yhbC, ygbP, ybeY, gcpE, kdtB, pfs, ycaJ, b1808, yeaA, yagF, b1983, yidD, yceG and/or yjbC, the sequence of said genes being shown in Fig. 1, or a fragment, derivative or ortholog thereof, comprising the steps of:
 - (a) contacting a bacterial cell with said candidate antagonist or inhibitor or sample; and
 - (b) determining whether said contacting leads to cell growth inhibition and/or cell death resulting from eliminating the function of at least one of said genes.

3. A method for testing a candidate antagonist or inhibitor of the function of a gene essential for bacterial growth or survival wherein said gene is selected from the group consisting of ygbB, yfhC, yacE, ychB, yejD, yrfl, yggJ, yjeE, yiaO, yrdC, yhbC, ygbP, ybeY, gcpE, kdtB, pfs, ycaJ, b1808, yeaA, yagF, b1983, yidD, yceG and/or yjbC, the sequence of said genes being shown in Fig. 1, or a fragment, derivative or ortholog thereof, comprising the steps of
 - (a) contacting a bacterial cell comprising said gene with a candidate antagonist or inhibitor or a sample comprising a plurality of said candidate antagonists or inhibitors; and
 - (b) determining whether said contacting leads to cell growth inhibition and/or cell death resulting from eliminating the function of at least one of said genes.
4. The method of any one of claims 1 to 3 further comprising identifying an antagonist or inhibitor, optionally from said sample of candidate antagonists or inhibitors.
5. The method of any one of claims 1 to 4 wherein said inhibitor or antagonist is further improved by peptidomimetics or by applying phage display or combinatorial library technique step(s).
6. A method for designing an improved antagonist or inhibitor for the treatment of a bacterial infection or disorder or disease related to a bacterial infection comprising the steps
 - (a) identification of the binding site of an antagonist or inhibitor to the polypeptide ygbB, yfhC, yacE, ychB, yejD, yrfl, yggJ, yjeE, yiaO, yrdC, yhbC, ygbP, ybeY, gcpE, kdtB, pfs, ycaJ, b1808, yeaA, yagF, b1983, yidD, yceG and/or yjbC, the sequence of said genes being shown in Fig. 1, or obtained by or identified by the method of any one of claims 1 to 5 by site-directed mutagenesis and chimeric polypeptide studies;
 - (b) molecular modeling of both the binding site of said antagonist or inhibitor and the structure of said polypeptide; and

- (c) modification of said antagonist or inhibitor to improve its binding specificity or affinity for the polypeptide.
7. An antagonist or inhibitor of the activity of a polypeptide encoded by a gene selected from the group consisting of ygbB, yfhC, yacE, ychB, yejD, yrfI, yggJ, yjeE, yiaO, yrdC, yhbC, ygbP, ybeY, gcpE, kdtB, pfs, ycaJ, b1808, yeaA, yagF, b1983, yidD, yceG and/or yjbC, the sequence of said genes being shown in Fig. 1, or fragment, derivative or ortholog thereof or of the expression of a gene encoding said polypeptide or said fragment, derivative or ortholog or obtained by or identified by the method of any one of claims 1 to 6.
 8. A method for producing a therapeutic agent comprising synthesizing the antagonist or inhibitor identified, tested or designed according to the method of any one of claims 1 to 6 or the antagonist or inhibitor of claim 7 or an analog or derivative thereof.
 9. A method for producing a composition comprising the steps of the method of any one of claims 1 to 6 or synthesizing the antagonist or inhibitor of claim 7 and formulating said inhibitor or antagonist in a pharmaceutically acceptable form.
 10. A composition comprising an antagonist or inhibitor of claim 7, the therapeutic agent produced by the method of claim 8 or the antagonist or inhibitor obtained by or identified in the method of any one of claims 1 to 6 or produced according to claim 9 and optionally a pharmaceutically acceptable carrier.
 11. The composition of claim 10 which is a pharmaceutical composition.
 12. The composition of claim 10 which is a kit.
 13. The composition of any one of claims 10 to 12 further comprising an antibiotic and/or cytokine.
 14. Use of a polypeptide encoded by a gene selected from the group consisting of ygbB, yfhC, yacE, ychB, yejD, yrfI, yggJ, yjeE, yiaO, yrdC, yhbC, ygbP, ybeY, gcpE, kdtB, pfs, ycaJ, b1808, yeaA, yagF, b1983, yidD, yceG and/or yjbC, the sequence of said genes being shown in Fig. 1, or a fragment, derivative or ortholog thereof or of any of said

genes for the identification of an antagonist or inhibitor of the activity of said polypeptide or said fragment, derivative or ortholog or of the expression of a gene encoding said polypeptide or said fragment, derivative or ortholog.

15. Use of an antagonist or inhibitor of claim 7, the therapeutic agent produced by the method of claim 8 or the antagonist or inhibitor obtained by or identified in the method of any one of claims 1 to 6 or produced according to claim 9 or identified by the use of any of the claims for the preparation of a pharmaceutical composition for the treatment of (a) bacterial infection(s), disorder(s) and/or disease(s) related to bacterial infections.
16. A method for treating or preventing bacterial infections or diseases or disorders related to bacterial infections comprising the step of administering to a subject in need thereof the antagonist or inhibitor obtained by or identified in the method of any one of claims 1 to 6 or produced according to claim 9 optionally comprised in the pharmaceutical composition according to claim 11.
17. Use of a polypeptide encoded by a gene selected from the group consisting of ygbB, yfhC, yacE, ychB, yejD, yrfI, yggJ, yjeE, yiaO, yrdC, yhbC, ygbP, ybeY, gcpE, kdtB, pfs, ycaJ, b1808, yeaA, yagF, b1983, yidD, yceG and/or yjbC, the sequence of said genes being shown in Fig. 1, or a fragment, derivative or ortholog thereof or any of said genes for screening for polypeptides interacting with said polypeptide using protein-protein interaction technologies, and/or for validating such interaction as being essential for bacterial survival and/or for screening for antagonists or inhibitors of such interaction.
18. Use of a polypeptide encoded by a gene selected from the group consisting of ygbB, yfhC, yacE, ychB, yejD, yrfI, yggJ, yjeE, yiaO, yrdC, yhbC, ygbP, ybeY, gcpE, kdtB, pfs, ycaJ, b1808, yeaA, yagF, b1983, yidD, yceG and/or yjbC, the sequence of said genes being shown in Fig. 1, or a fragment, derivative or ortholog thereof or any of said genes for screening of polypeptide for polypeptide binding to said polypeptide, and/or for validating the peptides binding to said polypeptide as preventing growth of bacteria or being lethal to bacteria upon expression of said polypeptides in said bacteria, and/or for screening for small molecules competitively displacing said peptides.

19. Use of conditional mutants in a gene selected from the group consisting of ygbB, yfhC, yacE, ychB, yejD, yrfI, yggJ, yjeE, yiaO, yrdC, yhbC, ygbP, ybeY, gcpE, kdtB, pfs, ycaJ, b1808, yeaA, yagF, b1983, yidD, yceG and/or yjbC, the sequence of said genes being shown in Fig. 1, or a fragment, derivative or ortholog thereof or of surrogate ligands against said gene expressed in bacteria to induce a lethal phenotype in bacteria and/or for the analysis of said bacteria for surrogate markers by comparison of RNA or protein profiles in said bacteria with RNA or protein profiles in wild type bacteria, and/or the use of said surrogate markers for the identification of antagonists of the essential function of said gene.
20. A method for identifying or isolating a surrogate marker comprising the steps as described in claim 19.
21. A method for identifying or isolating a surrogate marker comprising the steps of
 - (a) inducing a lethal phenotype in bacteria containing a conditional mutant of a gene selected from the group consisting of ygbB, yfhC, yacE, ychB, yejD, yrfI, yggJ, yjeE, yiaO, yrdC, yhbC, ygbP, ybeY, gcpE, kdtB, pfs, ycaJ, b1808, yeaA, yagF, b1983, yidD, yceG and/or yjbC, the sequence of said genes being shown in Fig. 1; and
 - (b) analysing said bacteria comparing the RNA or protein profile of said bacteria with wild type bacteria.